Identification of $C5a_{des\ arg}$ and an Anionic Neutrophil-Activating Peptide (ANAP) in Psoriatic Scales

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Scales from patients with nonpustular psoriasis were investigated for the presence of peptides capable of activating functional activities in human polymorphonuclear leukocytes (PMNL). Two compounds with similar molecular weight (12,500 and 15,000) were isolated which markedly stimulated PMNL functional activities including chemotaxis, generation of superoxide radical anion (O_2^-), and liberation of β-glucuronidase as a marker enzyme. As revealed by ion-exchange and subsequent radioimmunoassay followed by chromatofocusing, one peptide proved to be the desarginated form of the complement split product $C5a_{des\ arg}$. No C5a was detectable.

As a second psoriatic scale chemotaxin we isolated an anionic neutrophil-activating peptide (ANAP) which shows a single isoelectric point at pH 6.8. This peptide shares some of the characteristics of epidermal cell-derived thymocyte-activating factor and interleukin 1 and, as shown by deactivation experiments, it cross-reacts with a monocyte-derived cytokine. The 2 newly described neutrophil-activating peptides ($C5a_{des\ arg}$ and ANAP) may play an important role in the psoriatic tissue reaction. *J Invest Dermatol 87:53–58, 1986*

One of the intriguing aspects of the inflammatory tissue reaction in psoriasis consists in polymorphonuclear leukocytes (PMNL) migrating transepidermally toward the keratogenous zone [1]. Whereas these alterations histologically are clearly defined, the biochemical mediators participating in these events are not well known. In recent years lipid-like [2,3] as well as peptide-like [4,5] compounds with the capacity to stimulate PMNL were seen in psoriatic epidermis including scales.

Concentrating on peptide-like mediators, Tagami et al [6] found a chemotactic factor which was called "psoriatic leukotactic factor" (PLF). This factor was shown to possess some of the characteristics of the complement split product C5a [6].

Because in psoriasis as well as in other inflammatory skin diseases identification of the principal mediators with neutrophil-activating capacity may help to further understand the disease pathomechanism, we have investigated psoriatic scales for the presence of PMNL-activating peptides. We were able to identify $C5a_{des\ arg}$ as well as an anionic peptide as potent activators of neutrophil functions.

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Abbreviations:
ANAP: anionic neutrophil-activating peptide
BSA: bovine serum albumin
C5a: complement split product
ETAF: epidermal cell-derived thymocyte-activating factor
FMLP: formylated tripeptide
Il-1: interleukin 1
IP: isoelectric point
MOC: monocyte-derived chemotactic factor
O_2^-: superoxide radical anion
PAF: platelet-activating factor (C_{18})
PBS: phosphate-buffered saline, 0.04 M sodium phosphate, 0.254 M NaCl, pH 7.3
PMNL: polymorphonuclear leukocytes

MATERIALS AND METHODS

Crude scales were collected in a total of 9 patients with untreated psoriasis vulgaris. Diagnosis of psoriasis was well established by clinical criteria and all patients were hospitalized for subsequent treatment. Between 2–10 g crude scales were collected from each patient.

Preparation of Scale Extracts The scales (2–10 g) were suspended in 200 ml phosphate-buffered saline (PBS), pH 7.4, and homogenized using an ultraturrax for 10 min in an ice bath.

The homogenate was centrifuged (1000 *g* for 30 min), the supernatant was filtered through a 0.45-μm filter and thereafter the filtrate was concentrated 50-fold using Amicon YM 5 filters (Amicon Corp.) and stored below −70°C for chromatography.

Preparation of PMNL Polymorphonuclear leukocytes from healthy donors were isolated as previously described [7] using a slight modification of the method of Henson [8]. Using this technique final cell preparations contained more than 90% neutrophils with a viability of greater than 97% as assessed by trypan blue exclusion.

Chemotactic and Random Migration Chemotactic and random migration of PMNL were assayed using a modification of the "endogenous component chemotactic assay (ECCA)" method described by Creamer et al [9] using β-glucuronidase as marker enzyme.

Production of Superoxide Anions (O_2^-) Superoxide anion-production was measured using a slight modification of the method described by English et al [10].

In order to ascertain proper controls, superoxide dismutase (bovine blood, Sigma, Munich, 1 mg/ml PBS) was added to control tubes in each experiment prior to the addition of cells to stop the reduction of cytochrome C by O_2^- [11].

Reduced cytochrome C was assayed in supernatants by measuring the extinctions at 550 and 540 nm (Hitachi 150-20 spec-

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trophotometer) vs blanks containing superoxide dismutase at the start of the reactions. O_2^- concentrations were calculated using an extinction coefficient of 15.5/mM × cm (ferrocytochrome C minus ferricytochrome C) [10].

When O_2^- production elicited by G-75 fractions was measured, 8×10^6 neutrophils per assay (total volume: 1 ml) were used after preincubation (10 min, 37°C) with cytochalasin B (5 μg/ml).

Enzyme Release

β-Glucuronidase Release: The marker enzyme of PMNL azurophilic granules, β-glucuronidase, was measured as described previously [12]. A 100% control was obtained by addition of 100 μl 0.2% Triton X-100 instead of the stimulus. Release of β-glucuronidase was expressed in percent of the Triton X-100-control (= 100%).

Myeloperoxidase Release: The second marker enzyme of PMNL azurophilic granules, myeloperoxidase, was measured as described by Pember and Kinkade [13]. In this assay *o*-phenylendiamin-dihydrochloride instead of guajacol was used as substrate. A 100% control was obtained by addition of 100 μl 0.2% hexadecyl-trimethylammonium-bromide (Sigma) in water instead of the stimulus.

Lactoferrin Release: Lactoferrin—a marker protein of PMNL secondary granules—was measured by enzyme-linked immunosorbent assay (ELISA) using a modification of the method recently described by Vilja et al [14]. Briefly, in this system affinity-purified antihuman lactoferrin-IgG antibodies (Miles GmbH, Frankfurt, F.R.G.) were used, which were coupled with biotin-N-succinimide. Biotin antibodies bound to lactoferrin were determined by avidin-peroxidase. This assay allowed measurement of low amounts (50 pg) of lactoferrin released from activated neutrophils. A 100% control was obtained by additions of PBS instead of the stimulus and 3-fold freezing and thawing. Release of lactoferrin was expressed in percent of the frozen/thawed (3 ×) control.

Chemotactic Factors Purified C5a was prepared according to a combination of the methods described by Fernandez and Hugli [15] and Beebe et al [16] as described earlier [17]. $C5a_{des\ arg}$ was prepared in a similar manner, however in the absence of the serum carboxypeptidase N-inhibitor ε-amino caproic acid. Both compounds showed different elution pattern, when chromatofocused at polybuffer exchanger PBE 9/11 with Polybuffer 8–10.5 for elution. Column fractions were assayed for O_2^- stimulating capacity with neutrophils.

A chemotactic factor derived from adherent monocytes (MOC) was obtained according to the method described for isolation of interleukin 1 (Il-1) in the absence of serum [18]. Briefly adherent mononuclear leukocytes were stimulated with *Escherichia coli* lipopolysaccharide (10 μg/ml) (Sigma) as well as silica (10 μg/ml) in medium RPMI for 24 h at 37°C.

Supernatants were concentrated using Amicon YM 5-ultrafilters and chromatographed on Sephadex G-75. Fractions, which stimulated migration of test neutrophils, were collected (M_r ~12,500), concentrated with YM 5-filters, and pooled below −70°C. This adherent monocyte-derived chemotaxin (MOC) stimulated migration, release of β-glucuronidase, peroxidase, and lactoferrin as well as reduction of cytochrome C of human neutrophils.

Sephadex G-75 Chromatography Concentrated scale extracts were chromatographed on Sephadex G-75 gel (column: 2.5 × 65 cm, Pharmacia, Uppsala, Sweden) with PBS (pH 7.2) at 4°C and separated into 5-ml fractions. After adding $CaCl_2$ and $MgCl_2$ (final concentrations of 1.3 and 1.0 mM, respectively), fractions were tested for migration stimulating activity, O_2^--generating activity, as well as β-glucuronidase- or myeloperoxidase-liberating activity with test neutrophils. As molecular markers, blue dextran, bovine serum albumin (BSA), complement fragment C5a, cytochrome C, as well as vitamin B_{12} were used and the eluted compounds were detected spectrophotometrically at 280 nm. The position of marker C5a was estimated by peak neutrophil-O_2^- production.

When necessary, fractions were concentrated by use of YM-5 membranes.

Chromatofocusing Fractions of G-75 chromatography activating PMNL functions at the M_r range 10,000–20,000 were concentrated and diafiltered with the appropriate starting buffer.

Chromatofocusing was done in 2 pH-intervals: for alkaline chromatofocusing, a column of polybuffer exchanger (PBE 118) was equilibrated with 0.025 M triethylamine-HCl and elution performed using Pharmalyte pH 8–10.5 (Pharmacia, Uppsala, Sweden) obtaining a pH gradient from pH 10.5–pH 8. For acidic chromatofocusing, a column of polybuffer exchanger (PBE 94) was equilibrated with 0.025 M imidazole-HCl and elution performed using polybuffer 74-HCl obtaining a pH-gradient within pH 7 and 4.

Fractions were concentrated using centricon 10-microconcentrators (Amicon GmbH, Witten, F.R.G.) and equilibrated with PBS. Thereafter they were tested for biologic activity (stimulation of migration, O_2^- production or enzyme release) using test neutrophils.

Ion-Exchange Chromatography G-75-chromatography fractions which activated PMNL functions (M_r range 10,000–20,000) were equilibrated with 0.005 M sodium phosphate, 0.002 M EDTA, pH 7.8, and then applied to a small column (2 × 0.5 cm) of CM-50-Sephadex, which was equilibrated with the same buffer. The column was washed with 10 ml equilibration buffer. Bound substances eluted with 10 ml 0.2 M glycine-HCl buffer, containing 1 M NaCl, pH 2.5, and fractions were immediately neutralized using solid Tris. Both pools with the basic as well as acidic components were diafiltered against PBS using Amicon YM-5 filters, concentrated, and tested for biologic activity as described.

Deactivation Experiments In some experiments, stimulus-specific deactivated neutrophils were used as test cells. For this purpose neutrophils were preincubated either with C5a or with partially purified MOC for 20 min at 37°C. Thereafter cytochalasin B was added giving a final concentration of 5 μg/ml and cells were incubated for an additional 5 min. Then fractions were added and incubated for 30 min at 37°C. After centrifugation the supernatants were tested for β-glucuronidase activity.

Controls were performed using C5a, MOC, and formylated tripeptide (FMLP) as stimuli. In all cases deactivation was stimulus-specific as revealed by the lack of inhibition of enzyme release in cells exposed to other stimuli at optimal concentrations.

Radioimmunoassay (RIA) for C5a and $C5a_{des\ arg}$ In the column fractions as well as crude scale extracts $C5a_{des\ arg}$ was determined using a commercial RIA kit (Upjohn GmbH, Heppenheim, F.R.G.) using the instructions of the manufacturer [19].

RESULTS

Separation of psoriatic scale extracts by G-75 chromatography revealed peak biologic activity in fractions which correspond to the M_r of 10,000–20,000 (Fig 1).

Biologic activity was seen with each of the functional parameters tested, e.g., stimulated migration, release of β-glucuronidase, and generation of O_2^-. In contrast to enzyme secretion and generation of O_2^- both of which showed 2 distinct peaks of activity (Fig 1), migratory activities were stimulated by a much wider range of fractions with one peak only.

Using PMNL which had been preincubated with C5a and, as seen in control experiments (data not shown) were in a deactivated state, these C5a-deactivated cells were then stimulated with scale fractions separated by G-75 chromatography. Fig 2 shows that enzyme release stimulated by near 12 kD fractions was nearly unaltered. However, degranulation eliciting activity was decreased when fractions corresponding to 15 kD were used as stimuli (Fig 2).

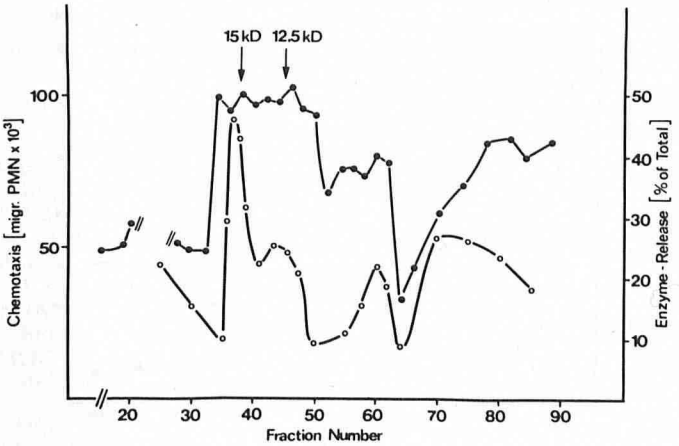

Figure 1. Sephadex G-75 chromatography of psoriasis scale extract. Neutrophil chemotactic activity (*solid circles*) as well as β-glucuronidase liberating activity in PMNL (*open circles*) were elicited by the column fractions. Peak elution of marker substances C5a (15 kD) and cytochrome c (12.4 kD) are indicated.

Fractions corresponding to 10–20 kD were subsequently examined for the presence of C5a or C5a$_{des\ arg}$ by radioimmunoassay. As shown in Fig 3, C5 split product(s) was present with peak activity corresponding to 15 kD (Fig 3). No C5a activity could be detected within the 12 kD fractions. In subsequent experiments the 10–20 kD fractions obtained by G-75-chromatography were chromatofocused within the pH range of 8–10.5. This system enabled us to separate C5a and C5a$_{des\ arg}$, the latter eluating at a lower pH than C5a. When the chromatofocusing column was reequilibrated, biologic activity eluted at the same position as authentic C5$_{des\ arg}$ (Fig 4). This is additional evidence that the 15 kD fractions contain desarginated C5a as a principal factor.

Characterization of the 12 kD Fraction Fractions within the 10–20 kD range were further characterized by Sephadex CM-50 ion-exchange chromatography. Preliminary experiments showed that the 10–20 kD-pool from G-75 chromatography contained chemotaxins which proved to be cationic as well as anionic. Subsequently fractions obtained by G-75 chromatography were divided into 2 pools (pool I and pool II) according to polarity (anionic or cationic peptides, Fig 5*a*). Pooled fractions of the 10–20 kD range were then separated by CM-50-Sephadex ion exchange and tested for biologic activity (Fig 5*b,c*).

Fractions with peak activity at 15 kD showed predominantly cationic behavior (Fig 5*b*) whereas the activity eluting later corresponded to acidic components (Fig 5*c*). In this way the 2 fractions revealing peak biologic activities were separated, resulting in a cationic component (evidently C5a$_{des\ arg}$) and a newly detected anionic factor with a slightly lower M_r.

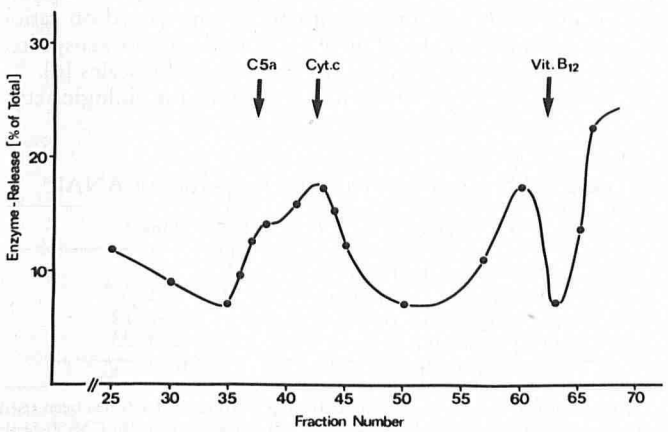

Figure 2. β-Glucuronidase liberating activity by G-75 chromatography fractions identical with those shown in Fig 1 using C5a-deactivated test neutrophils. Note loss of enzyme releasing activity in fractions 36–40.

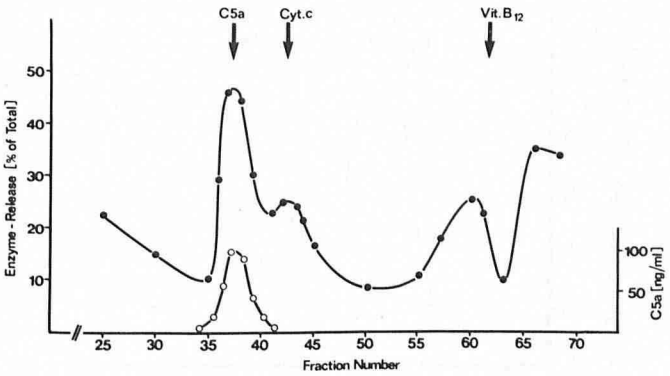

Figure 3. C5a radioimmunoassay (*open circles*) of G-75 chromatography fractions showing β-glucuronidase releasing activity (*solid circles*). Note that fractions containing highest amounts of C5a by radioimmunoassay correspond to fractions showing peak release of β-glucuronidase.

For further characterization, contaminating C5a$_{des\ arg}$ was absorbed using CM-50-Sephadex and the anionic components were chromatofocused in the pH range of 7.4–4.

To our surprise examination of these fractions for biologic activity revealed a single peak eluting at pH 6.8 (Fig 6). These fractions were able to elicit migratory activity in PMNL (data not shown) as well as the release of myeloperoxidase (Fig 6).

It should be mentioned that measurements of biologic activity of chromatofocusing fractions may be hampered by low ion contents as well as by different pH of the column fractions. In order to overcome such difficulties, large amounts of partially purified extracts (100 times the half maximal chemotaxis stimulatory doses) were chromatofocused. Also these fractions were concentrated as well as diafiltered against physiologic buffer. Under these conditions no additional activity peaks were seen to be present at lower elution pH.

Further characteristics of this peptide are shown in Table I. As can be seen from this table the factor activates O_2^- production,

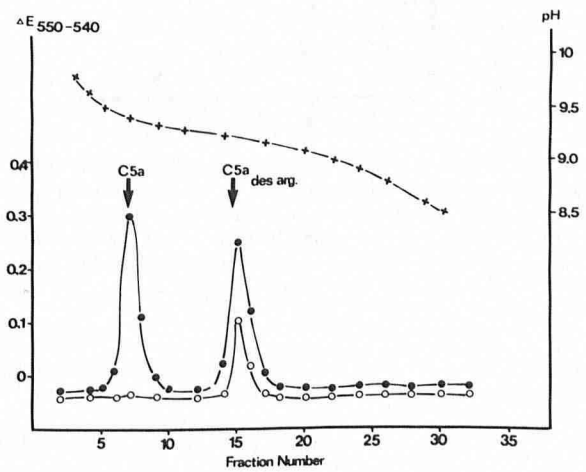

Figure 4. Chromatofocusing of partially purified cationic neutrophil-activating activity of a 10–20 kD G-75 chromatography pool from psoriatic scales. Cationic peptides of the 10–20 kD pool bound to CM-Sephadex were eluted with glycine buffer (pH 3) and these peptides were separated by alkaline chromatofocusing. The chromatofocusing column has been calibrated with authentic samples of C5a as well as C5a$_{des\ arg}$ (*solid circles*). Biologic activity of cationic psoriatic scale peptides (*open circles*) is present at the position of C5a$_{des\ arg}$. The pH is shown by *crosses*.

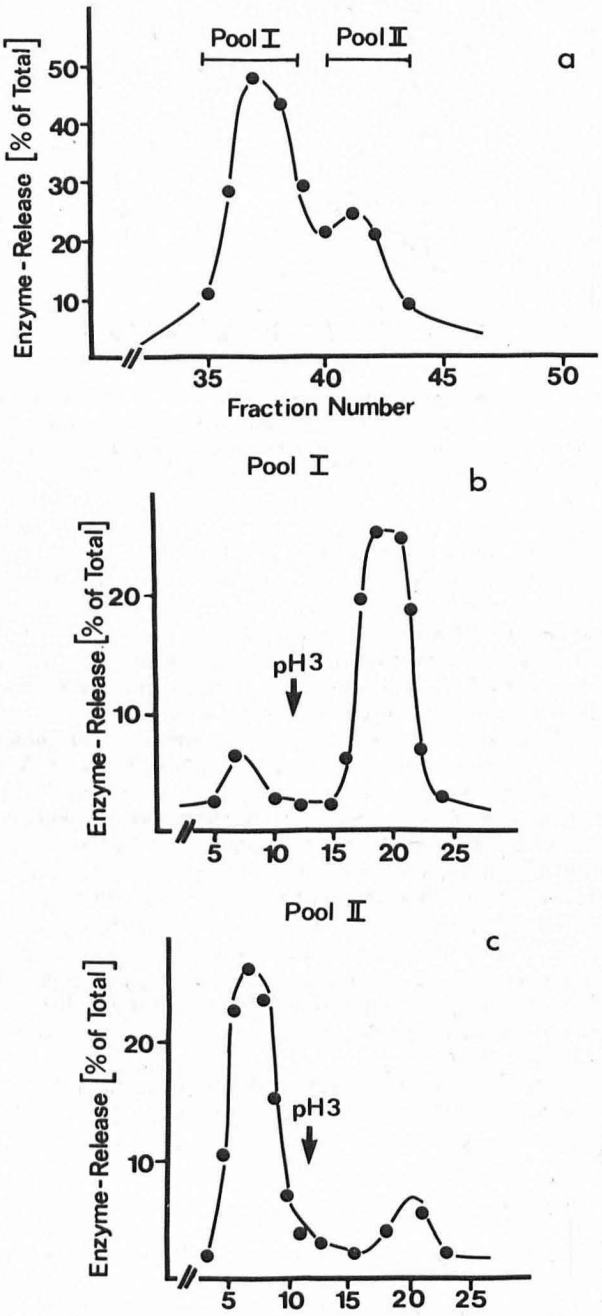

Figure 5. *a*, Fractions of G-75 chromatography within the range 10–20 kD were divided into pool I (peak near 15 kD) and pool II (peak near 12.4 kD). *b*, The activity profile of pool I when chromatographed on CM-Sephadex 50. It is notable that the main activity binds to the cation exchanger, which eluted at low pH. *c*, Pool II contains mainly compounds which do not bind to the cation exchanger.

release of β-glucuronidase, as well as myeloperoxidase and lactoferrin in cytochalasin B-treated neutrophils. In all our PMNL assays, this anionic neutrophil-activating factor (ANAP) produced typical dose-response curves (data not shown). When half-maximum eliciting doses for PMNL functional parameters were compared, chemotaxis was stimulated at much lower concentration as compared with O_2^- production and release of β-glucuronidase (Table I). The differences in concentrations (ED_{50}) were approximately 50-fold.

Deactivation Experiments Cells preincubated with ANAP and subsequently exposed to C5a, FMLP, PAF, and ANAP showed specific deactivation of enzyme release elicited by ANAP whereas

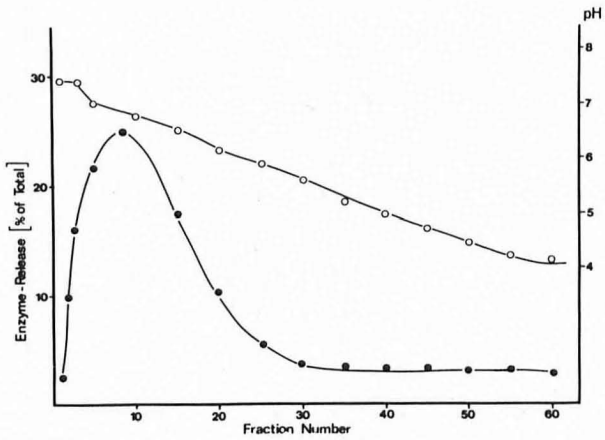

Figure 6. Chromatofocusing of partially purified anionic neutrophil activating component of a 10–20 kD G-75 chromatography pool from psoriatic scales. Anionic peptides of the 10–20 kD pool which did not bind to CM-Sephadex were separated by acidic chromatofocusing. Myeloperoxidase liberating activity (*solid circles*) of test neutrophils and pH (*open circles*) are shown. Prior to biologic test these fractions were diafiltered against PBS and concentrated.

no impairment of the enzyme-releasing activity was seen after stimulation with C5a, FMLP, or PAF (Table II). This indicates that ANAP apparently does not affect the receptor binding of these chemotaxins.

Finally, pretreatment of PMNL with a MOC [20] and vice versa clearly revealed cross deactivation for ANAP and MOC while full responses could be elicited with other chemotaxins (C5a, FMLP, and PAF) (Table II). In addition, pretreatment of neutrophils with MOC revealed the PMNL nonresponsive to ANAP (Fig 7), however not to other chemotaxins (Table II). These experiments indicate binding of both chemotaxins (MOC and ANAP) to the same chemotaxin receptor on neutrophils.

DISCUSSION

Using large amounts of scales obtained from patients with nonpustular psoriasis we were able to identify 2 compounds with similar M_r (12,500 and 15,000) which markedly stimulated neutrophil functions.

By ion-exchange chromatography one of these 2 components was found to be cationic and one was anionic. As revealed by radioimmunoassay and subsequently by chromatofocusing, the cationic psoriatic scale peptide proved to be the desarginated form of C5a ($C5a_{des\ arg}$).

In a chromatographic analysis of psoriatic scale extracts using Sephadex G-75 profiles Tagami and Ofuji [4] were able to identify fragments of the fifth complement component. Based on cation exchange chromatography of these fractions the authors suspected the presence of the anaphylatoxin C5a in psoriatic scales [6].

By assaying the chromatofocusing fractions for biologic activ-

Table I. Neutrophil Activating Properties of ANAP[a]

Function	Dose[b]
Chemotactic migration	1
Chemokinetic migration	1
β-Glucuronidase release	46 ± 12
O_2^- production	55 ± 23
Lactoferrin release	16 ± 7

[a]Partially purified anionic neutrophil-activating peptide (ANAP) has been used. Purification scheme: (a) G-75-chromatography of a scale extract; (b) CM 50-Sephadex-chromatography from a 10–20 kD G-75 pool. This preparation did not contain significant amounts of contaminating $C5a_{des\ arg}$.

[b]Arbitrary dose of ANAP necessary for half-maximum chemotactic stimulation. Results of 3 dose response studies performed in duplicate are shown.

Table II. Cross-Reactivity of PMNL Responses After Preincubation with Chemotaxins

	Stimulation with				
	C5a (10^{-8} M)	FMLP (1×10^{-8} M)	PAF (3×10^{-6} M)	ANAP (20 EC_{50})	MOC (20 EC_{50})
C5a 10^{-8}	28.6 ± 9.4	10.20 ± 9.4	83.1 ± 16.2	92.0 ± 9.6	89.0 ± 12.3
FMLP 1×10^{-8} M	97.1 ± 1.2	36.0 ± 11.1	88.0 ± 7.9	95.1 ± 5.4	93.0 ± 10.0
PAF 3×10^{-6} M	110.2 ± 14.3	117.5 ± 12.4	15.8 ± 4.5	115.4 ± 6.7	135.9 ± 10.0
ANAP 40 EC_{50}	100.0 ± 8.7	92.9 ± 7.6	100.0 ± 11.3	22.2 ± 2.3	26.9 ± 4.8
MOC 40 EC_{50}	100.4 ± 9.3	98.7 ± 5.8	110.6 ± 11.8	26.9 ± 4.2	23.5 ± 3.7

Enzyme release (β-glucuronidase) was determined in chemotaxin preincubated PMNL after subsequent stimulation with different chemotaxins. Results are expressed in percent of control. Note cross-deactivation by MOC and ANAP. Results of 2 triplicate experiments are shown.

Key: PMNL = polymorphonuclear leukocyte
C5a = complement split product
FMLP = formylated tripeptide
PAF = platelet-activating factor
ANAP = anionic neutrophil-activating peptide
MOC = monocyte-derived chemotactic factor

ity we were unable to identify any activity present at the elution position of C5a (Fig 4). Since a nearly 100-fold lower dose of C5a compared with $C5a_{des\ arg}$ is still sufficient to elicit chemotactic activity in PMNL [21], it appears unlikely that psoriatic scales contain any significant amounts of the anaphylatoxin C5a.

After generation of C5a by C5 convertase this anaphylatoxin is desarginated by carboxypeptidase N as the principal anaphylatoxin inactivator [22]. Loss of arginine reduces the anaphylactic activity of C5a nearly 1000-fold and this is known to take place within approximately 2 min in vivo [23]. In psoriasis any newly generated C5 fragments may take at least several hours or days to be present within scale products. Therefore it appears not to be surprising to detect desarginated C5a only.

Although $C5a_{des\ arg}$ is considerably weaker in PMNL stimulating activity as compared with C5a, the *large* quantities now detected in psoriatic scales may still be of importance in the pathogenesis of psoriasis. In addition, $C5a_{des\ arg}$ was not detectable in normal stratum corneum nor in scales from other scaling disorders including ichthyosiform erythroderma (Schröder, unpublished data). This suggests that complement activation plays a role in the psoriatic tissue reaction.

This concept is indirectly supported by a recent study on neutrophil functions in inflammatory skin diseases. Using C5a as well as a variety of other chemotaxins we were able to show that several patients with active psoriasis showed a specific absence of PMNL responses to C5a [17]. At the same time PMNL functions elicited by FMLP, LTB_4, or PAF remained unaltered.

This was taken as evidence that in active psoriasis complement activation with generation of C5 split products is a significant feature. At present it is not known exactly where the generation of C5 split products takes place, whether in the dermis or within the epidermis, nor do we know by what pathway complement becomes activated. Still, the presence of comparatively large amounts of $C5a_{des\ arg}$ within the horny layer in psoriasis is intriguing considering the various effects of this powerful cytotaxin in PMNL as well as in eosinophils, mast cells, basophils, or lymphocyte subsets [24].

The second scale chemotaxin identified here is an acidic compound which elutes with a slightly lower M_r as compared with $C5a_{des\ arg}$ (Fig 1). Anionic neutrophil-activating compounds in the range of 10–20 kD have not been described before in psoriatic scales. This could be due to technical reasons since characterization of chemotactic peptides from psoriatic scales on the basis of charge are impeded by drastic loss of yields in chemotactic activity [6].

For several reasons this ANAP appears to be different from neutrophil-activating peptides such as ETAF [25] or Il-1 [18] and leukocytic pyrogen [26].

First, peak activity of ETAF derived from human epidermal cell cultures was found between 15–30 kD [25]. Also as shown in a recent study, the M_r of highly purified Il-1 was near 17,000 [27]. These data differ markedly from the 12.5 kD seen for ANAP in our present study.

Second, differences exist with regard to the isoelectric point (IP). For human ETAF 3 IPs have been described [25] and similarly, for highly purified Il-1 3 IPs have been shown [27]. On the other hand, human ETAF demonstrating defined chemotactic activity has been found to show only 2 IPs [28]. In these studies ETAF as well as Il-1 differed not only with regard to the number but also with regard to the position of their IP. In contrast the anionic scale peptide (ANAP) detected here showed only a single IP at pH 6.8.

The reasons for these discrepancies are not clear at the moment. In fact, these peptides may represent a heterogenous group of mediators which, as stated by Luger et al [28], may differ in their final structure but have a region in common. The anionic scale peptide (ANAP) described in this study could thus belong to this family of peptide cytokines including the monocyte-derived factor MOC.

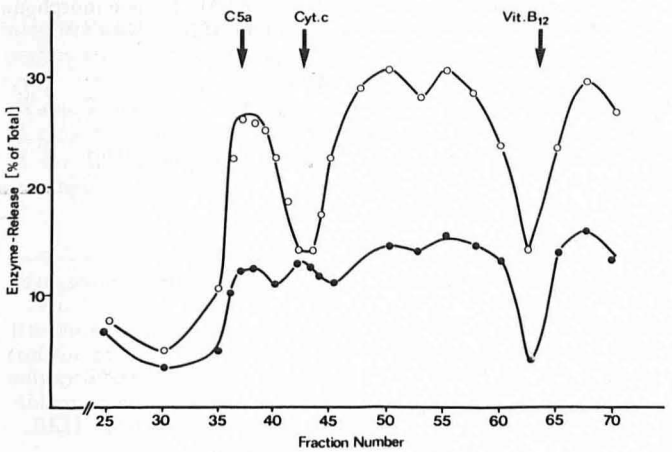

Figure 7. β-Glucuronidase liberating activity in fractions off G-75 chromatography using control (*open circles*) and neutrophils deactivated by MOC (*solid circles*). Note the lowered response to fraction 43 which corresponds to the elution volume of the marker cytochrome c.

It is noteworthy that in addition to psoriatic scales we were able to extract ANAP from normal stratum corneum (callus) as well as from scales in patients with ichthyosiform erythroderma (Schröder, unpublished data). At present the role of this peptide in epidermal biology is not known, and also studies of the release mechanisms of this neutrophil-activating cytokine are needed.

Taken together, our study shows that psoriatic scales contain 2 newly defined neutrophil-activating peptides with marked biologic activities. Their presence within the epidermis may be related to pathogenic pathways not yet fully explored.

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